

### **REMARKS/ARGUMENTS**

Applicants would like to thank the Examiner for the careful consideration given the present application. The application has been carefully reviewed in light of the Office Action, and amended as necessary to more clearly and particularly describe the subject matter that Applicants regard as the invention.

Applicants acknowledge that the Examiner has withdrawn the species elections with regard to Fraction A and Fraction C of Quillaja saponin Fraction A. Applicants acknowledge that claims 3, 11, 16, 17, and 19 are withdrawn. Applicants note that claims 3 and 11 depend from claims 1 and 9, respectively. Accordingly, on allowance of claims 1 and 9, rejoinder and allowance of the claims 3 and 11 is respectfully requested pursuant to the Office's rejoinder procedure. MPEP § 821.04.

Claims 1, 8, and 14 have been amended to more clearly describe the invention, as explained below.

New dependent claims 20-23 have been added. With regard to these claims, the dependencies place these claims within elected claim group 1. With regard to the claims that read upon the elected aspects, it is to be appreciated that all of the claims read upon (b) at least one antigenic molecule. It should be appreciated that although all of the claims do not specifically state an antigenic molecule, none of the claims explicitly excludes the presence of an antigenic molecule.

No new matter has been entered. Basis for the amendments can be found in the specification as filed. Regarding claims 22-23 in particular, the composition MB703 comprises a mixture of Fraction A and Fraction C of Quillaja saponin Fraction A comprising 7 parts of A and

3 parts of C. Table 1. The composition MM703 was prepared by mixing Matrix A and Matrix C, wherein Matrix A corresponds to iscom matrix particles including Fraction A of Quillaja saponin Fraction A and Matrix C corresponds to iscom matrix particles including Fraction C of Quillaja saponin Fraction A. Thus, MM703 comprises a plurality of iscom particles comprising different Fractions of Quillaja saponin Fraction A.

The Examiner has rejected claims 1, 2, 4-8, and 18 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as his invention. The Examiner has cited two grounds of rejection.

First, the Examiner has rejected claims 1, 2, 4-8, and 18 based on lack of clarity regarding the scope of the claimed invention. Specifically, the Examiner states the following:

It is . . . not clear if the claim is implicitly requiring that the iscom particle be combined with the antigen composition to form a single composition comprising both the iscom and the antigen, or [i]f the claim is merely requiring that an iscom be used as an adjuvant without specifically requiring the combination of the iscom and the antigen prior to administration.

Office action, p. 4. Claim 1, as amended, is directed to a method of preparing an antigenic composition, comprising combining an iscom particle and at least one live micro-organism. The rejection of claim 1 is therefore respectfully submitted to be overcome. Moreover, claims 2, 4-8, and 18 each depend from claim 1, either directly or indirectly, and accordingly the rejection of these claims is also respectfully submitted to be overcome.

Second, the Examiner has rejected claims 8 and 14 based on lack of clarity regarding the meaning of “subfragment A or subfragment C o[f] Quillaja saponin Fraction A.” Office action, p. 4. Claims 8 and 14, as amended, are directed to a method and a composition, respectively, wherein the iscom particle comprises at least one of Fraction A and Fraction C of Quillaja

saponin Fraction A. The rejection of claims 8 and 14 is therefore respectfully submitted to be overcome.

The Examiner has rejected claims 1, 2, 6, 9, 10, and 15 under 35 U.S.C. § 102(b) as being anticipated by Wechter et al., U.S. Pat. No. 6,177,081. Specifically, the Examiner has stated that “Wechter teaches live attenuated viruses for use in vaccines,” that “[t]he reference teaches the combination of the attenuated viruses with an iscom,” and that “the reference also inherently teaches claim 6” since “iscoms are known in the art to comprise glycosides and lipids.” Office action, p. 5. As can be seen, the Examiner has compared the vaccines of Wechter with the compositions and methods as claimed in claims 1, 2, 6, 9, 10, and 15. Respectfully, the two are not the same. Specifically, claim 1, as amended, is directed to a method of preparing an antigenic composition, based on combining an iscom particle and at least one living micro-organism, and claim 9 is directed to a composition comprising at least one iscom particle and at least one living micro-organism. In contrast, Wechter teaches the use of a live attenuated virus as a starting material for antigen incorporation into an iscom particle, said use inevitably involving production steps that will kill any virus or other micro-organism, and thus Wechter does not teach any composition that includes an iscom particle and a live micro-organism or any method for making such a composition.

More specifically, Wechter relates to an isolated and purified marmoset or human activating virus and to compositions comprising the virus, as indicated in Wechter claims 1 and 4, respectively. The compositions of Wechter include the whole virus, as well as portions of the virus. *See* col. 5, ll. 33-34. Wechter discusses different types of portions and polypeptides obtained from the virus. Cols. 5 to 9. Wechter indicates that live attenuated viruses also can be incorporated into iscoms for use as a vaccine using methods well known in the art. Col. 9, ll. 29-

31. However, the incorporation of a virus, although starting from a live micro-organism, inevitably involves production steps that will kill the micro-organism. Wechter also discusses the presentation of viral coat protein antigens in iscoms, col. 9, ll. 36-37, which are parts of the killed micro-organism. Further, Wechter cites a Nature article from 1984 authored by one of the Applicants. Col. 9 ll. 43-44. It was already known at that time to start the production of iscom particles from whole micro-organisms. However, again, the micro-organisms were inevitably killed during the production process. Thus, Wechter fails to teach any composition that includes an iscom particle and a live virus, or any other live micro-organism. In contrast, according to the present invention as claimed in claims 1, 2, 6, 9, 10, and 15, an iscom particle or iscom matrix particle is combined with a live micro-organism in a single composition without incorporation of the live micro-organism into the iscom particle and without killing of the live micro-organism. The rejection of claims 1 and 9 is therefore respectfully submitted to be overcome. Moreover, claims 2 and 6 both depend from claim 1 and claims 10 and 15 depend from claim 9 and accordingly the rejection of these claims is also respectfully submitted to be overcome.

The Examiner has rejected claims 1-2, 6-8, and 18 under 35 U.S.C. § 102(b) as being anticipated by Iosef (Vaccine 20: 1740-53). Specifically the Examiner indicated that “claim 1 merely requires the use of an iscom particle as an adjuvant” and “does not appear to specifically require the combination of the iscom with the live microorganism.” Office action, p. 5. As can be seen, the Examiner has compared the Iosef method of separately administering an iscom vaccine and a live virus vaccine with the method as claimed in claim 1. Respectfully, the two are not the same. As noted above, claim 1, as amended, is directed to a method of preparing an antigenic composition, comprising combining an iscom particle and at least one live micro-organism. In contrast, as stated by the Examiner, “Iosef teaches methods for the induction of

immune responses in pigs comprising the administration of both a live attenuated virus, and the administration of a non-infectious VLP/iscom vaccine.” Office action, p. 6. The Examiner specifically and correctly concedes that “the reference does not teach the combination of iscom with the live virus.” Office action, p. 6. The rejection of claim 1 is therefore respectfully submitted to be overcome. Moreover, claims 2, 6-8, and 18 depend from claim 1, either directly or indirectly, and accordingly the rejection of these claims is also respectfully submitted to be overcome.

The Examiner has rejected claims 1, 2, 5-10, and 13-15 under 35 U.S.C. § 103(a) as being unpatentable over Wechter in view of Morein et al. (U.S. Pat. No. 5,679,354). Specifically, the Examiner states that “[w]hile Wechter teaches the incorporation of attenuated viruses into iscoms, it does not specify the formula of the iscoms.” Office action, p. 7. The Examiner then argues that “Morein provides teachings relating to iscoms for use as an adjuvant for antigens.” Office action, p. 7. Respectfully, the incorporation of attenuated viruses into iscoms is not the same as making an antigenic composition by combining an iscom and at least one live micro-organism, for the reasons indicated above. To reiterate, the incorporation of an attenuated virus into an iscom necessarily involves killing the virus, the resulting product being iscom particles that include parts of a killed virus, not a composition comprising an iscom and a live virus or other live micro-organism. As indicated above, Wechter does not teach any antigenic composition comprising an iscom and at least one live micro-organism. Morein also does not teach such a composition. Thus, the combination of Wechter and Morein does not make obvious the inventions as claimed in claims 1 and 9. The rejection of claims 1 and 9 is therefore respectfully submitted to be overcome. Moreover, claims 2, 5-8, 10, and 13-15 depend

from claims 1 or 9, either directly or indirectly, and accordingly the rejection of these claims is also respectfully submitted to be overcome.

The Examiner has rejected claims 7, 8, 13, and 14 under 35 U.S.C. § 103(a) as being unpatentable over Wechter in view of Morein as applied to claims 1, 2, 5, 6, 9, 10, 13, and 15, and further in view of Cox et al. (WO 96/11711). Specifically, the Examiner states that “the teachings of Wechter and Morein do not specifically refer to the use of isolated Fractions A and C of Quil A” but that “Cox teaches similar iscom formulations to those of Morein and indicates that preferred embodiments of such iscoms use as glycosides Fractions A and C of Quil A.” Office action, p. 8. The rejection is impliedly based on an assumption that the combination of Wechter and Morein makes obvious an antigenic composition comprising an iscom and at least one live micro-organism. Again, for the reasons indicated above, the combination of Wechter and Morein does not make obvious such an antigenic composition. The rejection of claims 7 and 13 is therefore respectfully submitted to be overcome. Moreover, claims 8 and 14 depend from claims 7 and 13, respectfully, and accordingly the rejection of these claims is also respectfully submitted to be overcome.

The Examiner has rejected claims 1, 2, 4, 9, 10, 12, 15, and 18 under 35 U.S.C. § 103(a) as being unpatentable over Van Woensel et al. (U.S. Pat. No. 5,925,359). The Examiner states that “Van Woensel teaches a composition for the vaccination of pigs comprising live attenuate[d] PRRS viruses” and “that the composition[] may be combined with an adjuvant.” Office action, p. 8. The Examiner states that the reference “specifically suggests the incorporation of the live vaccine antigens in iscoms.” Office action, p. 8. The Examiner also states that “the reference suggests the additional combination of live[] attenuated vaccines with other antigens, including antigenic material (i.e. antigenic molecules) from other pathogens.” Office action, p. 8.

Respectfully, as is the case with the Wechter reference, Van Woensel does not teach making a composition by combining an iscom particle and at least one live micro-organism, and thus Van Woensel does not make obvious the inventions as claimed in claims 1 and 9. Specifically, Van Woensel relates to a vaccine based on a live attenuated Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) of a European serotype, which is not infectious to macrophages. According to claim 8 of Van Woensel, the vaccine may further comprise one or more non-PRRSV attenuated or inactivated pathogens or antigenic material thereof. Van Woensel states that an adjuvant and, if desired, one or more emulsifiers such as Tween and Span may also be incorporated in the live attenuated vaccine according to the invention. Col. 5 ll. 13-19. Suitable adjuvants include, for example, vitamin E acetate solubilisate, aluminium hydroxide, aluminium phosphate or aluminium oxide, (mineral) oil emulsions such as Bayol and Marcol52, and saponins. Incorporation of the antigens in iscom is also a possible way of adjuvation. Thus, it is the antigenic material of attenuated or inactivated pathogens that is incorporated into iscom. The incorporation requires treatment of the pathogen in order to free hydrophobic components from the pathogen. Such a treatment, which again is required for incorporation into an iscom, will kill any pathogen. The rejection of claims 1 and 9 is therefore respectfully submitted to be overcome. Moreover, claims 2, 4, 10, 12, 15, and 18 depend from claims 1 or 9, and accordingly the rejection of these claims is also respectfully submitted to be overcome.

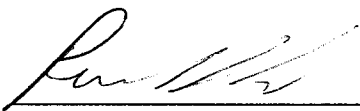
The Examiner has rejected claims 5-8 and 13-14 under 35 U.S.C. § 103(a) as being unpatentable over Van Woensel as applied to claims 1, 2, 4, 9, 10, 12, 15, and 18, and further in view of Cox et al (WO 96/11711). The Examiner states that "Van Woensel teaches compositions comprising an attenuated live virus and an iscom" and "that the compositions may comprise additional antigens." Office action, p. 9. The Examiner also states that "Cox teaches

that iscoms may be in the forms of iscoms comprising the glycosides and lipids identified in the rejected claims” and “that iscom matrices may be used which incorporate an immunogen.” Office action, p. 9. Respectfully, as indicated above, neither Van Woensel nor Cox teach a composition comprising an iscom particle and at least one live micro-organism. Thus, the combination of Van Woensel and Cox does not make obvious the inventions as claimed in claims 5-8 and 13-14. The rejection of claims 5-8 and 13-14 is therefore respectfully submitted to be overcome.

In light of the foregoing, it is respectfully submitted that the present application is in condition for allowance and notice to that effect is hereby requested. If it is determined that the application is not in condition for allowance, the Examiner is invited to initiate a telephone interview with the undersigned attorney to expedite prosecution of the present application.

If there are any additional fees resulting from this communication, please charge same to our Deposit Account No. 16-0820, our Order No. ALBI-41848.

Respectfully submitted,  
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